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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/749,706	SCHREINER ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's response of 14 February has been received and entered. Claims 1, 2 and 4 have been amended and claims 11-12 have been added. Claims 1-12 are currently pending and under examination in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 14 February 2007 have been fully considered but are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 9-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Guyton (Textbook of Medical Physiology, 8th edition, W.B. Saunders Company, pages 209-218, 1991) in view of Roberts et al. (J. Cell Sci. 108: 2369-2379, 1995) for the reasons of record in the previous Office action.

Applicant argues that there is no motivation to combine the two references. Applicant asserts that Roberts et al. teaches they were unable to determine whether VEGF administration would cause protein efflux as well as small solute efflux. Applicant also asserts that neither reference teaches the identification of a patient suffering from decreased renal solute filtration or excretion.

Applicant's arguments have been fully considered, but are not persuasive. The only patient population identified by Applicant as suffering from "decreased renal solute filtration or excretion" are those suffering from hypertension. Therefore, the recitation of "a patient suffering from decreased renal solute filtration or excretion" is essentially, a patient suffering from hypertension. Therefore, the prior art teaches the identification of the claimed patient population.

Guyton teaches that in individuals with essential hypertension, the "kidneys will not excrete adequate amounts of salt and water unless the arterial pressure is high" (see page 217, column 2, item #7). Essential hypertension is generally treated by giving drugs that (1) increase renal blood flow and/or (2) decrease tubular reabsorption of salt and water (see page 218, column 1, paragraph 2). Roberts et al. teach that VEGF is a growth factor which has mitogenic effects on endothelium and occurs as 4 isoforms (121, 165, 189 and 206 amino acids). Roberts et al. also teach that VEGF induces endothelial fenestrae and increases vascular permeability to solutes. Roberts et al. also teach that fenestrated endothelium normally occurs in the capillaries of kidney glomeruli and that fenestrated capillary endothelium is more permeable to water and small solutes than continuous endothelium. One would be motivated to use VEGF

because Guyton teaches that individuals with essential hypertension have an impaired ability to excrete salt and water and because Roberts et al. teach that VEGF functions to increase the permeability of endothelium and that the kidney glomeruli have fenestrated endothelium. One would have a reasonable expectation of success because Roberts et al. teach that fenestrated capillary endothelium is more permeable to small solutes and VEGF would stimulate fenestration of this tissue. Therefore, the invention as a whole would have been *prima facie* obvious at the time the invention was made, absent evidence to the contrary.

Applicant also argues that Roberts et al. does not teach that VEGF administration causes small solute efflux in the absence of protein efflux and that the skilled artisan would be dissuaded from using VEGF because of this possible effect. This argument is not persuasive Klanke et al. (cited by Applicant; Nephrol. Dial. Transplant. 13: 875-885, 1998) teach that protein excretion is unchanged by VEGF/VPF administration (see abstract).

Claims 1-7 and 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guyton (Textbook of Medical Physiology, 8th edition, W.B. Saunders Company, pages 209-218, 1991) in view of Roberts et al. (J. Cell Sci. 108: 2369-2379, 1995) further in view of Zioncheck et al. (U.S. Pat. No. 6,485,942) for the reasons of record as applied to claims 1-7 and 9-10.

Applicant argues that Guyton and Roberts do not support a prima facie case of obviousness, and that Zioncheck et al. does not overcome the shortcomings of Guyton

and Roberts. Applicant also argues that there is no motivation to use heparin-free forms of VEGF in view of Roberts et al.

Applicant's arguments have been fully considered, but are not found persuasive. The applicability of Guyton and Roberts has been addressed above. Regarding Zioncheck, the advantages of using VEGF121 are stated in Zioncheck (i.e. slower rates of clearance). Applicant argues that there is no motivation to use heparin-free forms of VEGF in light of Roberts et al.'s comments on page 2377. However, there are no comments that specifically state that a VEGF with a modified heparin binding domain would not be functional. One would be motivated to use VEGF121 or a form of VEGF with a modified heparin binding domain because Zioncheck et al. teach that these VEGF molecules have a slower rate of clearance from the body. Additionally, one of ordinary skill in the art would be motivated to use more than one type of VEGF because therapeutics are often used where different forms with different clearance rates are desirable, resulting in a bolus dose and a maintenance effect. One would have a reasonable expectation of success in treating hypertension and increasing excretion of salt and water because Roberts et al. teach that fenestrated capillary endothelium is more permeable to small solutes and VEGF would stimulate fenestration of this tissue. Therefore, the invention as a whole would have been *prima facie* obvious at the time the invention was made, absent evidence to the contrary.

Claims 1 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Guyton (Textbook of Medical Physiology, 8th edition, W.B. Saunders Company,

pages 209-218, 1991) in view of Roberts et al. (J. Cell Sci. 108: 2369-2379, 1995) further in view of Cid et al. (U.S. Pat. No. 5,318,957) for the reasons of record in a previous Office action.

Applicant argues that Cid et al. does not cure the deficiencies of Guyton and Roberts et al. Applicant's argument has been fully considered, but is not persuasive. Guyton and Roberts et al. have been discussed above. Applicant argues that Cid et al. is silent to treating hypertension with angiogenic factors. However, Cid et al. teach that angiogenic factors are useful for treatment of conditions which involve angiogenesis, and Guyton teach that hypertension can cause a number of conditions which involved angiogenesis.

In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/083,817. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to treatment of hypertension by the administration of VEGF. The base claims differ in wording, but the patient population which is being treated is the same and the same protein is being administered, therefore, the claims are not patentably distinct.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,352,975. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current claims and the claims of the issued patent are

directed to methods of treating hypertension using VEGF. The instant claims focus on a mechanism of action, which includes increased excretion of a solute from the kidney, but this process would be inherent to the administration of VEGF in a patient with hypertension, therefore, the claims are not patentably distinct from each other.

Applicant did not provide any arguments regarding these rejections. The rejections are maintained for the reasons of record.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud